UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

MEMORANDUM

DATE: June 28, 2021

SUBJECT: Efficacy Review for HP2O2,
EPA Reg. No. 45745-11
Action Code Case: 00216417 – Electrostatic Spray
E-submission No. 60348

FROM: Nicole Karikari
Nicole Karikari
Efficacy Branch
Product Science Branch
Antimicrobials Division (7510P)

THRU: Kristen Willis, Chief
Kristen Willis
Efficacy Branch
Antimicrobials Division (7510P)
Date Signed: June 28, 2021

TO: Aline Heffernan, PM 31
Regulatory Management Branch I
Antimicrobials Division (7510P)

APPLICANT: Midlab, Inc.

Formulation from the Label:

Active Ingredient(s)	% by wt.
Hydrogen Peroxide	4.25%
Other Ingredients	95.75%
Total	100.0%

I BACKGROUND

Product Description (as packaged, as applied): Concentrated Liquid (Dilutable)

Submission type: Label Amendment

Currently registered efficacy claim(s): Dilutable disinfectant (bactericidal, virucidal, and fungicidal) product for hard, nonporous surfaces.

Requested action(s): The registrant is requesting conditional registration for a label amendment to add electrostatic sprayer claims. The registrant agrees to submit additional data at a later date.

Documents considered in this review:

- Cover letter from applicant to EPA dated 2/16/2021
- Proposed label dated 2/11/2021
- Data Matrix (EPA Form 8570-35) dated 2/16/2021
- Two efficacy studies (MRIDs 51352702, 51352703)
- One efficacy discussion (MRIDs 51352701)
- Confidential Statement of Formula (EPA Form 8670-4)
    - Basic Formulation dated 6/17/2016

II PROPOSED DIRECTIONS FOR USE

"**To Prepare Use Solution:**
Add the product at 2 oz. of product per gallon of water (1:64).
§For Use as a (Daily) (One-Step) Cleaner/Disinfectant:
• Dilute at 2 oz. of product per gallon of water (1:64)
• Pre-clean visibly soiled surfaces.
• Apply Use Solution with a (sponge, brush, cloth,) (mop,) (low pressure mechanical spray device,) (or) (hand pump)(coarse trigger) sprayer to hard, non-porous surfaces. Spray 6 - 8 inches from surface, making sure to wet surfaces thoroughly.
• All surfaces must remain visibly wet for ten (10) minutes.
• Wipe surfaces (or let air dry).

Use (4 oz.) or (8 oz.) per gallon of water to kill Enterococcus *faecalis* (Vancomycin Resistant (VRE)**.** ***(To be used if VRE is used as a kill claim.)***
Use (2.5 oz) or (2.5-4) per gallon of water to kill *Listeria monocytogenes* (ATCC19117) (***To be used if Listeria monocytogenes is used as a kill claim*.)**
Use 8 oz. per gallon of water to kill *Trichophyton interdigitale (*Athlete's foot fungus). ***(To be used if Trichophyton interdigitale is used as a kill claim.)***

For use as a *Virucide:
• Dilute at 2 oz. of product per gallon of water (1:64)**:**
• Pre-clean visibly soiled surfaces.
• Apply Use Solution until thoroughly wet to hard, non-porous surfaces.
• All surfaces must remain visibly wet for five (5) minutes. A one (1) minute contact time is required for *HIV-1 (AIDS virus), *Influenza Virus Type A (H1N1), *††SARS-Related Coronavirus 2 (the virus that causes COVID-19), †*Avian Influenza A (H7N9) virus. **(Virus to be listed if used as a kill claim.)**

• Wipe surfaces (or let air dry).

(Use 2 oz. or 4 oz. of product per gallon of water to kill Avian Influenza A (H7N9) virus

GENERAL DIRECTIONS FOR USE WITH [(ELECTROSTATIC SPRAYER APPLICATION) (APPLICATOR/SPRAYER NAME)]:
Note: Consider material compatibility and potential for damage prior to application.
• Place signs or warning indicators outside the treatment area to indicate that treatment is in progress.
• Ensure that bystanders and pets are not present in the area to be treated.
• Put on appropriate PPE. At a minimum, this must include safety glasses, gloves and N95 mask.
• Follow manufacturer's instructions for sprayer use. Spray droplet particle size should be set to limit volume median diameter of ≥40µm.
• Place the electrostatic spray function in the ON position for electrostatic spray models that have the functionality to toggle ON/OFF.
• Wiping is not required to ensure surface disinfection; however, you may choose to wipe specific surfaces to polish them (e.g., glass, mirrors) or to remove visible residue after the contact time is achieved.
• Individuals may enter area 30 minutes after treatment.

For Use as a One-Step Cleaner/Disinfectant by Electrostatic Spraying: Dilute at 2 oz. of product per gallon of water (1:64). Pre-clean visibly soiled surfaces. Apply Use Solution with electrostatic sprayer to hard, non-porous surfaces. Spray 18 - 24 inches from surface, making sure to wet surfaces thoroughly. All surfaces must remain visibly wet for ten (10) minutes. Let air dry or wipe surfaces to polish.
For use as a *Virucide by Electrostatic Spraying: Dilute at 2 oz. of product per gallon of water (1:64). Pre-clean visibly soiled surfaces. Apply Use Solution with electrostatic sprayer to hard, non-porous surfaces. Spray 18 - 24 inches from surface, making sure to wet surfaces thoroughly. All surfaces must remain visibly wet for ten (10) minutes. Let air dry or wipe surfaces to polish."

III AGENCY STANDARDS

EPA expedited review for adding electrostatic spray application directions:
https://www.epa.gov/pesticide-registration/expedited-review-adding-electrostatic-spray-application-directions-use

Per 2018 810.2200 guideline, testing for viruses should be conducted using ASTM E1053. In a deviation from the guideline, EPA requested 3 product lots at the LCL be tested for SARS-CoV-2.

Per the discussion included in MRID 51352701 dated 2/16/2021:

"GLP efficacy studies using the currently registered product, HP2O2, EPA Reg. No. 45745-11, were tested at ALG with an electrostatic spray device as the method of application.

The lots used in testing were characterized under GLP with percent of hydrogen peroxide results as follows:

Lot	GLP COA Value
618201	4.24%
618202	4.32%
518203	4.30%
1112191	4.31%
1112192	4.26%

Based on the COA values, the lots were diluted accordingly to ensure they met the Lower Certified Limit (LCL) concentration at the 1:64 dilution ratio for efficacy testing. The two studies submitted with this action were initiated prior to the Agency-issued August 2020 guidance "Expedited Review for Adding Electrostatic Spray Application Directions for Use to Antimicrobial Product Registrations." Midlab approached the testing at ALG as a confirmatory efficacy testing using an electrostatic sprayer with the AOAC Germicidal Spray Test Method, testing on 60 carriers each against *Pseudomonas aeruginosa, Salmonella enterica,* and *Staphylococcus aureus*. Confirmatory testing was also conducted using an electrostatic sprayer in the ASTM E1053 Virucidal Efficacy Test and Feline calicivirus, as the hardest to kill virus on the product label. However, in all testing, only one spray distance was used.

Please see the enclosed email to Kristen Willis, dated January 20, 2021, requesting the Agency accept the generated data on the main bacteria and Feline calicivirus as presented. In the subsequent pages, images of the separate wetness testing study are presented.

This acceptance is requested with the condition that Midlab provide additional electrostatic spray data following the Agency issued guidance. Midlab has requested protocols and is awaiting testing in queue to confirm the results already obtained."

On 1/20/2021, the consultants (SRC, Inc.) on behalf of the registrant (Midlab) sent the following email to the EPA (K. Willis).

From: CMaira@SRCConsultants.com <CMaira@srcconsultants.com>
Sent: Wednesday, January 20, 2021 9:48 AM
To: Willis, Kristen <Willis.Kristen@epa.gov>
Cc: rjones@srcconsultants.com; rmannion@srcconsultants.com
Subject: Outreach on Behalf of Midlab - Proposed ESS Amendment

Hi Kristin,

I am reaching out to you on behalf of our client, Midlab, regarding their registered product, HP2O2, EPA Registration #45745-11. This hydrogen peroxide-based product is listed on List-N with a 1 minute contact time.

In May of 2020, Midlab initiated a GLP virucidal study at ALG, testing two lots of their HP2O2 product at LCL against Feline calicivirus (FCV) using the GST modified to have the application conducted with an electrostatic sprayer (ESS). At that time, they were working under the assumption that ESS would simply be a different application method and thus they set out to do confirmatory studies using the ESS as the means of application. They achieved a ≥ 6-$\log_{10}$ reduction in the FCV and proceeded to schedule testing at ALG for 3 lots of product to be tested against *Pseudomonas aeruginosa, Staph aureus,* and *Salmonella enterica.* When the protocols were requested and signed, the guidance had not yet been published by EPA for ESS.

As such, they had GLP studies conducted with only one specified spray distance of "18 to 24 inches" using a Victory Electrostatic Sprayer set at 110 micron particle size. They tested 2 lots of chemically characterized product at LCL against FCV (2 carriers each lot) and 3 lots of chemically characterized product at LCL vs. PA, SA, and SE. They tested 60 carriers for each organism and each lot of product in the bacterial efficacy testing, rather than just the 10 carriers that are required for confirmatory testing. All of the studies have valid, passing data which is summarized in the table below.

Study #	Lab	GLP?	Lot #	Organism	Hard Water	Soil	Te
A30046	ALG	Yes	1112191 1112192	FCV	400 ppm AOAC hard water	5%	GST (mo ESS a
A30698	ALG	Yes	618201 618202 618203	PA, SA, SE	400 ppm AOAC hard water	5%	GST (mo ESS a

As you may already know, the GLP labs are just starting to conduct the ESS testing in accordance with the guidance issued by EPA in late summer 2020. Midlab has already requested protocols to have the ESS studies repeated utilizing two spray distances (5" and 24"), however, the lab schedule is several months out from now.

Therefore, we would respectfully request that the Agency consider allowing Midlab to submit an Amendment to EPA Registration #45745-11 to add the Electrostatic Spray Application to their product with expedited review based on the GLP data that they have developed. We understand that this would be a Conditional Registration and that it would be

necessary to submit passing data at the required two distances as soon as the testing is completed. The required wetness test has already been conducted at ALG at distances of 5" and 24" with a contact time of 9 min, 45 seconds. The wetness testing was conducted as a non-GLP study and the results for the gravimetric and physical wetness determination procedure were both passing, where the acceptance criterion is visual wetness of the Kim Wipe used on each carrier and a weight following the exposure time that is greater than the dried weight for each carrier tested.

Thank you in advance for your consideration and please feel free to contact me if you have any questions or would like to discuss any of this further.

Best regards,
Crystal

Crystal Maira, Consultant
Scientific & Regulatory Consultants, Inc.
201 W. Van Buren Street | Columbia City, IN 46725
www.srcconsultants.com | 260.244.6270

On 1/20/2021, the EPA (K. Willis) sent the following email response to the consultants (SRC, Inc.) on behalf of the registrant (Midlab).

From: Willis, Kristen <Willis.Kristen@epa.gov>
Sent: Wednesday, January 20, 2021 10:14 PM
To: CMaira@SRCConsultants.com <CMaira@srcconsultants.com>; Pham, Thao <Pham.Thao@epa.gov>
Cc: rjones@srcconsultants.com <rjones@srcconsultants.com>; rmannion@srcconsultants.com <rmannion@srcconsultants.com>
Subject: RE: Outreach on Behalf of Midlab - Proposed ESS Amendment

Hi Crystal,
We would definitely consider the application based on the description below with the understanding that the additional studies would be submitted at a later date. Please include a copy of this email with the submission.

Thanks,
Kristen

On 1/20/2021, the consultants (SRC, Inc.) on behalf of the registrant (Midlab) sent the following reply email to the EPA (K. Willis).

From: CMaira@SRCConsultants.com <CMaira@srcconsultants.com>
Sent: Wednesday, January 20, 2021 10:56 PM
To: Willis, Kristen <Willis.Kristen@epa.gov>; Pham, Thao <Pham.Thao@epa.gov>
Cc: rjones@srcconsultants.com; rmannion@srcconsultants.com
Subject: Re: Outreach on Behalf of Midlab - Proposed ESS Amendment

Hi Kristen,

Thank you so much for your quick response and your consideration of this application. May I also confirm that this amendment will still be eligible for expedited review as well?

Best regards,
Crystal

Crystal Maira, Consultant
Scientific & Regulatory Consultants, Inc.
201 W. Van Buren Street | Columbia City, IN 46725
www.srcconsultants.com | 260.244.6270

On 1/21/2021, the EPA (K. Willis) sent the following email response to the consultants (SRC, Inc.) on behalf of the registrant (Midlab).

From: Willis, Kristen <Willis.Kristen@epa.gov>
Sent: Thursday, January 21, 2021 10:25 AM
To: CMaira@SRCConsultants.com; Pham, Thao
Cc: rjones@srcconsultants.com; rmannion@srcconsultants.com
Subject: RE: Outreach on Behalf of Midlab - Proposed ESS Amendment

Confirming that the application is eligible for expedited review.

Thanks,
Kristen

III STUDY SUMMARIES

1.	**MRID**	51352702
Study Objective		Disinfectant – Bactericidal when applied by an electrostatic sprayer
Testing Lab; Lab Study ID		Analytical Lab Group – Midwest; A30698
Experimental Start Date		9/9/2020 **Study Completion Date:** 10/27/2020
Test organism(s) **☐ 1 ☐ 2 ☒ 3 ☐ 4+**		*Pseudomonas aeruginosa* (ATCC 15442) *Salmonella enterica* (ATCC 10708) *Staphylococcus aureus* (ATCC 6538)
Test Method		AOAC Germicidal Spray Method (modified for ESS), Protocol Number: MDL01080420.GS.2
Application Method		The electrostatic sprayer (Victory Innovations) was primed for 5-15 seconds (see protocol deviations) before use with the particle size set to large and electrostatic set to on. Test carriers were sprayed in a horizontal position at a distance of 18-24 inches from the electrostatic sprayer held at a 45º angle (see protocol deviations).
Test Substance Preparation	**Name/ID**	HP2O2
	Lots **☐ 1 ☐ 2 ☒ 3**	0618201 0618202 0618203
	Preparation	Tested concentration: LCL Tested Dilution: 2 oz. per gallon defined as 1 ml test substance + 67.2 ml 400 ppm AOAC Synthetic Hard Water (Lot 0618201); 1 ml test substance + 68.5 ml 400 ppm AOAC Synthetic Hard Water (Lot 0618202); and 1 ml test substance + 68.2 ml 400 ppm AOAC Synthetic Hard Water (Lot 0618203)
Soil load		5% Fetal Bovine Serum (FBS)
Carrier type, # per lot		Glass slides, 60 per lot
Test conditions		Contact time: 9 minutes 58 seconds Temperature: 18-19°C Relative humidity: 36-52% (*Pseudomonas aeruginosa*); and 44-52% (*Salmonella enterica* and *Staphylococcus aureus*)
Neutralizer		Letheen Broth + 0.1% Sodium Thiosulfate + 0.01% Catalase
Reviewer comments (i.e. protocol deviations and amendments, retesting, control failures, etc.)		No Protocol Amendments were reported. Protocol Deviations: • For testing performed on 9/24/2020, the carrier population control for *Pseudomonas aeruginosa* failed to meet 5.0 Log_{10} CFU/carrier against Lot 0618202. The testing for Lot 06182020 against *Pseudomonas aeruginosa* was determined invalid by the laboratory and testing was repeated on 10/12/2020. The invalid data from 9/24/2020 is documented in Attachment I.

	• The protocol for the use of the electrostatic sprayer included in the study indicates that the sprayer should be held at an approximate 45º angle from 18-24 inches while spraying the carriers. For testing performed on 9/9/2020, the technician did not document the angle the sprayer was held but documented the spraying distance of 18-24 inches. • The protocol for the use of the electrostatic sprayer included in the study states that the sprayer should be primed by spraying the prepared product for 15 seconds before use and between lots. In addition, the protocol indicates that the sprayer should be rinsed with deionized water by spraying for 5 seconds between lots and post testing. For the testing on 9/24/20 and 10/12/2020, the technician primed the sprayer with prepared product for 5 seconds before testing and between lots, and that sprayer was rinsed with deionized water by spraying for 5 seconds between lots and post testing.

2.	**MRID**	51352703		
Study Objective		Disinfectant - Virucidal when applied by an electrostatic sprayer		
Testing Lab; Lab Study ID		Analytical Lab Group – Midwest; A30046		
Experimental Start Date		7/10/2020	**Study Completion Date:**	7/29/2020
Test organism(s) **☒ 1 ☐ 2 ☐ 3 ☐ 4+**		Feline Calicivirus strain F-9 (ATCC VR-782) as a surrogate for Norovirus		
Indicator Cell Culture		Crandek Reese feline kidney (CRFK) cells (ATCC CCL-94)		
Test Method		ASTM E1053-20 Standard Practice to Assess Virucidal Activity of Chemicals Intended for Disinfection of Inanimate, Nonporous Environmental Surfaces; MDL01051120.FCAL		
Application Method		The carriers were sprayed for 8 seconds, until thoroughly wet, at a distance of 18-24 inches with the sprayer held at approximately a 45º and held covered for the contact time. Between each lot of test substance, the sprayer was rinsed with sterile deionized water and sprayed into a sink for 5 seconds and then primed for 5 seconds with the next lot of test substance.		
Test Substance Preparation	**Name/ID**	HP2O2		
	Lots **☐ 1 ☒ 2 ☐ 3**	1112191 1112192		
	Preparation	Tested concentration: LCL Tested Dilution: 2 oz. per gallon defined as 1 oz. test substance + 68.32 oz. 400 ppm AOAC Synthetic Hard Water (Lot 1112191); 1 oz. test substance + 67.53 oz. 400 ppm AOAC Synthetic Hard Water (Lot 1112192)		
Soil load		5% Fetal Bovine Serum (FBS)		

Carrier type, # per lot	Glass Petri dish;
Test conditions	Contact time: 9 minutes 55 seconds Temperature: 20.0°C Relative humidity: 50%
Neutralizer	Sephadex LH-20 gel columns
Reviewer comments (i.e. protocol deviations and amendments, retesting, control failures, etc.)	Protocol Amendments: The protocol was amended to indicate the stability testing was or will be performed following 40 CFR Part 60 GLP regulations. No Protocol Deviations were reported.

IV STUDY RESULTS

Disinfection – Electrostatic Spray Bactericidal Efficacy

MRID	Organism	Results		Population Control Average Log_{10} CFU/ carrier
		Lot. No.	No. Exhibiting Growth/ Total No. Tested	
10 minutes, 2 oz. per gallon in 400 ppm AOAC hard water, 5% organic soil load				
51352702	*Pseudomonas aeruginosa* (ATCC 15442)	0618201	0/60	5.20
		0618202	0/60	5.69
		0618203	0/60	5.11
	Salmonella enterica (ATCC 10708)	0618201	0/60	4.97
		0618202	0/60	5.28
		0618203	1/60	5.31
	Staphylococcus aureus (ATCC 6538)	0618201	0/60	5.42
		0618202	0/60	5.52
		0618203	0/60	5.65

Disinfection – Electrostatic Spray Virucidal Efficacy

MRID	Organism	Description	Results				Dried Virus Control (Log_{10} $TCID_{50}$/carrier)
			Lot 1112191		Lot 1112192		
10 minutes, 2 oz. per gallon in 400 ppm AOAC hard water, 5% organic soil load							
51352703	Feline Calicivirus strain F-9 (ATCC VR-782) as a surrogate for Norovirus	Replicate	1	2	1	2	6.50
		10^{-1} to 10^{-4} dilution*	Complete inactivation		Complete inactivation		
		Log_{10} $TCID_{50}$/carrier	≤ 0.80		≤ 0.80		

MRID	Organism	Description	Results		Dried Virus Control (Log_{10} $TCID_{50}$/carrier)
			Lot 1112191	Lot 1112192	
10 minutes, 2 oz. per gallon in 400 ppm AOAC hard water, 5% organic soil load					
		Log_{10} Reduction	≥ 6.00	≥ 6.00	

*Post-neutralized samples were considered the 10^{-1} dilution.

Wetness Testing

In addition to the efficacy testing, the registrant performed wetness testing (non-GLP) to demonstrate that the surface remains visibly wet over the duration of the contact time. Images of the following weight measurements were provided.

MRID	Description	Weight
51352701	#1 TS1 15 sec	73.90 g
	#2 TS1 15 sec	75.96 g
	#3 TS1 15 sec	81.64 g
	#1 TS2 15 sec	92.14 g
	#2 TS2 15 sec	74.83 g
	#3 TS1 15 sec	72.20 g
	#1 TS1 5 sec	82.87 g
	#2 TS1 5 sec	75.93 g
	#3 TS1 5 sec	81.92 g
	#1 TS2 5 sec	93.57 g
	#2 TS2 5 sec	73.99 g
	#3 TS2 5 sec	92.39 g

V STUDY CONCLUSIONS

MRID	Claim	Surface Type	Application Method(s) and Dilution	Contact Time	Soil load	Diluent	Organism(s)	Data support tested conditions?
51352702	Disinfectant, bactericidal	Hard non-porous surface	Electrostatic spray; 2 oz. per gallon	10 minutes	5% FBS	400 ppm AOAC hard water	• *Pseudomonas aeruginosa (ATCC 15442)* • *Salmonella enterica (ATCC 10708)* • *Staphylococcus aureus* (ATCC 6538)	**Yes***
51352703	Disinfectant, virucidal	Hard non-porous surface	Electrostatic spray; 2 oz. per gallon	10 minutes	5% FBS	400 ppm AOAC hard water	• Feline Calicivirus strain F-9 (ATCC VR-782) as a surrogate for Norovirus	**Yes***

* A full set of confirmatory data should be submitted within 1-year consistent with the instructions in the expedited guidance for adding electrostatic spray (https://www.epa.gov/pesticide-registration/expedited-review-adding-electrostatic-spray-application-directions-use). Testing should include two spray distances (5" and 24").

VI LABEL COMMENTS

Label Date/Identification Number: 02/11/2021

1. The proposed label claims that the product, HP2O2, EPA Reg. No. 45745-11, when diluted at 2 oz. per gallon in 400 ppm water, is an effective disinfectant and virucide against the following on hard, non-porous surfaces in the presence of 5% organic soil for a 10-minute contact time when applied via electrostatic spray according to the appropriate directions for use. This is based on testing against the following:

   Pseudomonas aeruginosa (ATCC 15442)
   Salmonella enterica (ATCC 10708)
   Staphylococcus aureus (ATCC 6538)

   These claims are **partially acceptable** as additional data are needed to substantiate them.

2. Within 1-year, a full set of confirmatory data should be submitted to EPA consistent with the instructions in the expedited guidance for adding electrostatic spray (https://www.epa.gov/pesticide-registration/expedited-review-adding-electrostatic-spray-application-directions-use). As indicated in Section III (email correspondence between the registrant and the Agency (K. Willis)), additional studies and wetness testing should be conducted to align with the current EPA expedited review guidance for adding electrostatic spray application directions.

3. Make the following changes to the proposed label:
   a. Throughout the label,
      i. Revise "Multi-Surface/Multi Surface" to "Multi-Nonporous, Hard Surface" as data have only been submitted to the Agency to substantiate the use of this product on hard, nonporous surfaces.
      ii. Remove "cleaner disinfectant" and similar claims or qualify with "when used according to disinfection directions".